Comparison of effective dose and lifetime risk of cancer Incidence of CT attenuation correction acquisitions and radiopharmaceutical administration for myocardial perfusion imaging

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Comparison of Effective Dose and Lifetime Risk of Cancer Incidence of Computed Tomography Attenuation Correction Acquisitions and Radiopharmaceutical Administration for Myocardial Perfusion Imaging

Abstract
Objectives: To measure the organ dose and calculate effective dose from CTAC acquisitions from four commonly used gamma camera SPECT/CT systems.

Method: CTAC dosimetry data was collected using thermoluminescent dosimeters on GE's Infinia Hawkeye four and single slice systems, Siemen's Symbia T6 and the Philips Precedence. Organ and effective dose from the administration of ^{99m}Tc-tetrofosmin and ^{99m}Tc-sestamibi were calculated using ICRP reports 80 and 106. Using this data the lifetime biological risk was calculated.

Results: The Siemens Symbia gave the lowest CTAC dose (1.8 mSv) followed by the GE Infinia Hawkeye single-slice (1.9 mSv), GE Infinia Hawkeye four-slice (2.5 mSv) and Philips Precedence (3.0). Doses were significantly lower than the calculated doses from radiopharmaceutical administration (11 mSv and 14 mSv for 99m Tc-Tetrofosmin and 99m Tc-Sestamibi respectively). Overall lifetime biological risks were lower suggesting that using CTAC data posed minimal to the risk to the patient. Comparison of data for breast tissue demonstrated a higher risk than that from the radiopharmaceutical.

Conclusions: CTAC doses were confirmed to be much lower than from radiopharmaceutical administration. The localised nature of the CTAC exposure compared to the radiopharmaceutical biological distribution indicated dose and risk to the breast to be higher.

Advances in knowledge: This research proved that CTAC is a comparatively low dose acquisition. However, it has been shown that there is increased risk to breast tissue especially in the younger patient. As per legislation justification is required and CTAC should only be used in situations that demonstrate sufficient net benefit.

Introduction

SPECT/CT has become common place in clinical imaging and a major role for CT is for the attenuation correction (AC) of SPECT data in myocardial perfusion imaging (MPI) [1, 2]. The benefits of CTAC in MPI are well known and many national and international professional organisations recommend its use to improve SPECT MPI diagnostic accuracy [3, 4]. Associated with the CT acquisition is an additional radiation dose which is often considered to be low yet very few papers quantify the dose and the associated risk.

Effective dose is a useful figure that allows for a comparison between different techniques and protocols to be made. However it is widely recognised that the tissue weighting factors are averaged over both genders and all ages and so assessment and comparison of risk for an individual patient or patient group is not advised [5-8].Lifetime risk of cancer incidence, sometimes referred to as lifetime biological risk is a concept that has been suggested by a number of authors as an alternative to effective dose (*E*) to allow a comparison of risk from non-uniform dose distributions [5-7, 9]. Brenner [5-7] is arguably the strongest advocate for a move to what he terms “effective risk” as it is argued that *E* is based on “questionable science” as the tissue-specific weighting factors used, although based on research, are established by committee decisions and do not take into account differing age and gender dependencies. Wall et al [10] similarly states that *E* can and should play a role in radiation protection of radiation workers and members of the public and for the optimisation of techniques involving changes in radiation quality.

The quality of the images generated by CTAC and the clinical evaluation of these to identify incidental extracardiac findings has been discussed in literature [11-13]. Using phantom and human studies it has been shown that CTAC data has the potential to allow a reporter to identify extracardiac pathology. The accuracy and confidence has been shown to vary with the protocols used. This paper measured the organ dose and calculated the *E* from CTAC acquisitions from four different protocols. The protocols selected were those pre-set by manufacturers in four commonly

used SPECT-CT scanners and were considered to be suitable to produce data of adequate quality to allow attenuation and scatter correction. The aim was to establish what differences in dose exist from the different protocols when the data produced is used for the same purpose. Using this data the lifetime biological risk was calculated with a specific emphasis on the female breast. To contextualise these figures organ, *E* and lifetime biological risks from the administration of radiopharmaceuticals (^{99m}Tc Tetrofosmin and ^{99m}Tc Sestamibi) were calculated from data contained in ICRP reports 80 and 106 [14, 15]. Comparisons were also made to estimated doses using the dose length product (DLP) and published normalised values of effective dose per DLP [16].

Materials and Methods

Organ dose (H_T) was measured using thermoluminescent dosimeters (TLD-100 [LiF], Thermofisher Scientific Massachusetts), and E was calculated from these values using the ICRP 103 waiting factors [17]. TLDs were placed within critical organs in an adult CIRS ATOM dosimetry phantom (model no 701B, CIRS, Virginia, USA). Four SPECT/CT systems were selected due to the variations in the CTAC protocols. The systems included: GE Infinia Hawkeye (single slice), GE Infinia Hawkeye (4 slice) (GE Healthcare, Buckinghamshire UK), Siemens Symbia T6 (Siemens Healthcare Erlangen, Germany) and Philips Precedence (Philips Healthcare, Amsterdam, Netherlands).

The CIRS ATOM dosimetry verification phantom is made up of the head and torso of an adult male. There are thirty-nine contiguous slices containing differing density epoxy resin (representing bone, lung and soft tissue). The 701B is supplied with 5mm pre-drilled holes spaced in a 30 x 30 mm matrix that are filled with tissue equivalent plugs. Hole configuration had to be modified so that they aligned to specific internal organs. The modification was carried out by drilling additional holes as indicated in the phantom manufacturer's documentation for organ dosimetry [18].

The location and range to be scanned was established by performing CT scan of the phantom thorax and the upper and lower limit of the left ventricle identified. The scan range was measured and found to be 12 cm. The upper and lower borders of the scan range were marked on the phantom using permanent ink. Radiopaque markers were attached to the phantom to allow localisation on the scan projection radiograph (SPR) on the Siemens and Philips systems. The GE systems do not acquire an SPR as the operator uses the emission data to plan the CTAC range. Using a zero refresh rate on these scanners' positioning monitors a cobalt-57 source was placed on the marks for no more than five seconds to allow the scan range to be established. Using the reference activity of 3.7 MBq for the Cobalt source, the dose from this in 5 seconds at a distance of 1 cm in air would be 6.53 x 10^{-4} mGy. This value was considered to be negligible when calculating the dose from the TLDs in the phantom from the CTAC acquisitions.

Thermo-luminescent dosimeters (TLD-100) (Thermo Scientific, Erlangen, Germany) were cleaned and prepared in accordance with Tootell et al [19]. TLDs were organised into batches that ensured that the percentage variation of each batch was between 1.8 and 2.2 %. This was done by annealing and exposing all the TLDs to a uniform exposure of 120kV and 20mAs using a standard X-ray unit (Wolverson Arcoma, Willenhall, UK). The TLDs were ranked in order of response and organised into five batches. Each batch was calibrated using the same general X-ray unit at beam energies equivalent to the CTAC protocols using a calibrated Unfors Mult-O-Meter (Unfors RaySafe, Billdal, Sweden).

The TLDs were placed in a bespoke shielded case for transportation to the nuclear medicine departments involved in the study to prevent exposure to background radiation and any sources of radiation in the nuclear medicine departments. These TLDs were placed in the phantom in critical organs identified in ICRP 103 and the manufacturer user guide of the phantom to allow organ dose to be measured [17, 18, 20] (Table 1)

Table 1 Number of TLDs used in critical organs

Organ	Number of TLD
Adrenals	2
Bladder	16
Brain	11
Breast	2
Active bone Marrow	85
	Clavicle 20,
	Cranium 4
	Cervical Spine† 2
	Femora 4
	Mandible$^{\Diamond\times}$ 6
	Pelvis 18,
	Ribs 18
	Sternum 4

	Thoraco-lumbar Spine 9
Eyes*	2
Gall Bladder	5
Heart	2
Intestine (Small and large)	16
	Colon 11
	Small intestine 5
Kidneys	16
Liver	30
Lungs	36
Oesophagus	3
Pancreas	5
Prostate	3
Spleen	14
Stomach	11
Testes	2
Thyroid	10

* Not included in effective dose calculations

† TLDs located in the anterior of C2 and upper oesophagus were used to calculate extra thoracic organ dose

◊ TLDs located in the left and right lingula of the mandible and to the left and right of the sublingual fossa were used to calculate salivary gland organ dose

× TLDs located in the left and right lingula of the mandible were used to calculate oral mucosa organ dose

A total of five TLDs remained with the phantom except during imaging for background radiation correction. CTAC imaging was performed using the standard manufacturer protocols for MPI attenuation correction (Table 2).

Table 2 Protocols used for attenuation correction for myocardial perfusion imaging.

Scanner	Scout view	Axial/ Helical	kV	mA	Rotation	Slice thickness	Pitch	Automatic exposure/ dose modulation
GE Infinia Hawkeye (1 slice)	No	Axial	140	2.5	30 second per rotation (214^{o} exposure)	10mm	N/A	N/A
GE Infinia Hawkeye (4 slice)	No	Helical	140	2.5	30 second per rotation (214^{o} exposure)	5mm	1.9mm per rotation	N/A
Siemens Symbia T6	Yes	Helical	130	20	0.6s	3mm	0.938	AEC and DOM
Philips Precedence 16	Yes	Helical	120	30	1.5s	5mm	0.938	N/A

Three CTAC exposures were performed on each SPECT-CT system to allow a cumulative dose on the TLDs to be acquired. $CTDI_{vol}$ and dose length product data was recorded to be used for dose calculation and comparison to measured doses. Reading of the TLDs was carried out using a Harshaw 3500 manual TLD reader (Thermo Electron Corporation, Reading, UK) and WinRems software (Saint-Gobain Crystals & Detectors, Wermelskirchen, Germany). TLD readings were corrected for background and an average value for each TLD calculated. Organ doses were calculated and then used to calculate *E* and lifetime biological risk using the equations shown in Figure 1. The conversion coefficient for CT chest imaging was applied to the DLP readings and the resulting dosimetry compared to the measured readings [16].

Figure 1 Equations for (a) Organ dose, (b) Active bone marrow dose, (c) Effective dose and (d) Lifetime biological risk

a)

$$H_T = \frac{1}{n}\sum_{j}^{n} D_{i,j}$$

Where

H_T = equivalent organ dose
j = 1,…n, the number of TLDs in organ *i*.

b)

$$D_{abm} = \sum_{k} A_k \cdot D_k$$

Where

D_{abm} = Dose to active bone marrow
A_k = proportion of active bone marrow described by Cristy [21] ($\sum Ak = 1$)

c)

$$E = \sum_{T} W_T \cdot H_T$$

Where

E = effective dose to the entire body
W_T = tissue weighting factor of tissue (T) defined by ICRP 103 [20]
H_T = equivalent dose absorbed by tissue (T)

d)

$$R = \sum_{T} r_T \cdot H_T$$

Where

R = lifetime biological risk (defined as the generic lifetime radiation-attributable cancer risk)
r_T = lifetime radiation-attributable organ-specific cancer risk estimates (per unit equivalent dose to tissue T)
H_T = equivalent dose absorbed by tissue (T)

[18].

Active bone marrow dose was calculated using data on bone marrow distribution from Christy [21]. According to statistics, ischaemic heart disease affects a larger proportion of the population of men over 55 and women over 65 [22]. The maximum age considered by Christy is 40 therefore this data

was used in the equation for calculating the equivalent dose to active bone marrow.

Values for r_T used in this study are tabulated in the Health Protection Agency report HPA-CRCE-028 for 11 cancers of high risk organs over age ranges 0-9, 10-19, 20-29 etc. up to 90-99 [10]. Cancers of other radiosensitive organs share a collective risk estimate. This study followed the method described by Li et al [9] by applying this value to a weighted average dose of other radiosensitive organs (Figure 2).

Figure 2 Equivalent dose to Other Organs defined in ICRP 103[17]

$$H_{other} = \frac{\sum_{otherorgans} w_T \cdot H_T}{\sum_{otherorgans} w_T}$$

Other organs included the salivary glands, brain, heart, kidney, gallbladder, spleen, pancreas, adrenal glands, thymus, small intestine, extrathoracic region and oral mucosa. Data collection using TLDs for lymph nodes, muscle, bone surface and skin was not performed as they are large organs/systems and it was deemed these would contribute very little to the overall *E* and lifetime biological risk calculations as only a small proportion of the tissue would be exposed during the imaging process and their exclusion would have negligible effect. The weighting for the remaining organs was averaged over those organs where dose was measured [23].

Organ and *E* for the radiopharmaceutical administration were calculated using data provided in ICRP report 80, report 106, diagnostic reference levels (DRL) indicated in the Administration of Radioactive Substances Advisory Committee's publication and guidance published by the British Nuclear Medicine Society and adopted by the British Cardiac Society and the British Nuclear Cardiology Society [15, 24-26]. The total dose and risks for a stress and rest procedure using a total

1600MBq of ^{99m}Tc-tetrofosmin and ^{99m}Tc-sestamibi were compared to the additional dose and risk from the CTAC acquisitions performed using parameters described in Table 2. Data for lifetime biological risk incidence was obtained from Wall et al [10].

Results

Table 3 shows the dose effective dose for a single CTAC acquisition of the four protocols used in the study.

Table 3 Organ and Effective doses for a single CTAC acquisition measured using TLDs.

Organ	Dose (mSv)			
	GE Infinia Hawkeye 1	**GE Infinia Hawkeye 4**	**Siemens Symbia T6**	**Philips Precedence**
Brain	0.0	0.0	0.1	0.1
Salivary glands	0.0	0.0	0.1	0.2
Thyroid	0.1	0.3	0.8	0.4
Oesophagus	1.3	1.9	1.2	2.3
Lungs	1.8	2.7	1.5	2.8
Breast	3.5	3.3	2.0	4.1
Liver	1.3	2.4	1.3	2.4
Stomach	0.5	1.2	0.9	1.5
Colon	0.0	0.1	0.2	0.2
Bladder	0.0	0.0	0.2	0.2
Testes	0.0	0.0	0.1	0.2
Active (red) bone marrow	0.6	0.6	0.9	0.9
Remainder	0.1	0.1	0.1	0.1
Effective Dose	1.0	1.2	0.9	1.5

Table 4 shows the comparison in E measured using TLD and E calculated using the DLP.

Table 4 Effective dose using DLP*k (conversion coefficient (mSv/mGy*cm) where k=0.017 [16]

System protocol	$CTDI_{vol}$ (mGy)	DLP (mGy*cm)	Calculated Effective Dose (E_{DLP}) (mSv)	Measured Effective Dose (E_{TLD}) (mSv)	Percentage difference (%)

GE single slice	4.11	49	0.83	1.0	13.5
GE four slice	3.9	46	0.78	1.2	46.3
Siemens Symbia T6	1.75	21	0.36	0.9	85.7
Philips Precedence	3.5	42	0.71	1.5	71.5

E and organ dose for the lung, oesophagus, colon, liver and stomach from the administration of ^{99m}Tc Tetrofosmin and ^{99m}Tc Sestamibi are shown in Table 4 and two CTAC acquisitions (performed for both rest and stress protocol) are shown in Table 5.

Table5 Equivalent and effective doses following administration of radiopharmaceuticals for a rest/stress procedure and two CTAC acquisitions.

	Dose (mSv)					
	^{99m}Tc Tetrofosmin	^{99m}Tc Sestamibi	GE single slice	GE four slice	Siemens Symbia T6	Philips Precedence
Organ						
Lung	5.1	7.1	3.6	5.4	3.1	5.5
Oesophagus	5.3	6.5	2.5	3.8	2.4	5.6
Colon	28.8	34	0.2	0.2	0.6	0.5
Liver	5.3	16	2.6	4.7	2.7	4.9
Stomach	7.4	10	1.1	2.4	1.7	3.1
Breast	3.7	5.7	7.1	6.6	4.1	8.2
E (mSv)	11	13.3	1.9	2.5	1.8	3.0

Following the method described by Wall et al [10] conversion to lifetime cancer risk per million (10^6) was performed and are shown in Table 6.

Table 6 Total risk (per million) from radiopharmaceutical and CTAC acquisitions using diagnostic reference levels and manufacturer protocols

	Risk (per 10^6)			
	Age at exposure			
Examination	40-49	50-59	60-69	70-79
^{99m}Tc Tetrofosmin	525	386	244	130
^{99m}Tc Sestamibi	608	447	284	152
CTAC GE single slice	63	52	39	24
CTAC GE four slice	101	83	61	37
CTAC Siemens Sybmia T6	80	63	45	27
CTAC Philips Precedence	103	86	64	40

Consideration was given to the risk to the breast from radiopharmaceutical administration and CTAC acquisition. The phantom used in the study was male and no additional breast tissue was added however, the acquired data allowed for a comparison of the risks within the context of this study.

Table 7 Risk to breast (per million) from radiopharmaceutical and CTAC acquisitions using diagnostic reference levels and manufacturer protocols

	Risk (per 10^6)			
	Age at exposure			
Examination	40-49	50-59	60-69	70-79
^{99m}Tc Tetrofosmin	31	31	8	3
^{99m}Tc Sestamibi	48	48	12	5
CTAC GE single slice	60	60	15	6

CTAC GE four slice	55	55	14	5
CTAC Siemens Sybmia T6	34	34	9	3
CTAC Philips Precedence	69	69	17	6

Discussion

Comparison of E_{DLP} and E_{TLD} showed significant differences in the two values with E_{DLP} being consistently lower. This agrees with published literature [27-29]. However, the average percentage difference between the two is 54.2% which far exceeds figures quoted by Groves et al [27] of 18% and Hurwitz et al [29] of 25%. Criticisms of *k* state that the factors are based on old technology and old data; they are based on several scanners that were in use circa 1990 and the tissue weighting factors used in their calculation are from ICRP 60 [16, 30, 31]. There are also a number of assumptions made that would increase the error in the calculated effective dose. For example, the patient is assumed to be standard and, as noted by McCollough et al [32], this standard patient is a little thin by today's standards (nominal body mass of 70 kg). Possible sources of error were considered and additional quality checks performed on the TLDs. The batches were checked for uniformity and were found to be within the 2% level established before the experiment commenced at higher and lower doses of X-radiation. The images acquired as part of the CTAC exposure were also compared and it was clear that the same region of the phantom was exposed each time. Whether the cited criticisms of *k* are the main contribution to these differences is unclear from this research.

Comparing *E* of the CTAC acquisitions to those from the administration of the radiopharmaceuticals it can be seen that these figures are smaller but acquisition of AC data using CT does contribute additional dose to the patient. From this research this is in the magnitude of 7.3% to 27.3%. Comparison of CTAC to the "typical effective dose" for a CT chest of 6.6 mSv supports the popular opinion that CTAC is a low-dose CT procedure [10].

Consideration of risk again highlights large differences between the radiopharmaceutical and CTAC acquisition. When considered with the reported benefits of CTAC in improving the sensitivity and specificity it can be said that the reported benefits of attenuation and scatter correction using CT benefits do outweigh the risks [33-35].

A comparison of doses from the CTAC acquisitions showed some interesting findings. The protocol from the Siemens Symbia T6 gave the lowest *E*, this was significantly different to the protocols from the Philips Precedence and GE Hawkeye 4 slice systems (paired T Test, $p<0.05$). However statistical comparison of the protocols from the Symbia T6 to the GE Infinia Hawkeye single slice showed no statistical difference (paired T Test $p=0.37$). The Siemens Symbia T6 CT component is a higher specification system that has been shown to produce diagnostic quality CT images so it would be expected that *E* would be higher [12]. Close examination of the imaging parameters in Table 2 does highlight two interesting features, including the use of automatic exposure control (AEC) and dose modulation (DOM) during the acquisition. This technology (referred to as CARE Dose4D) manipulates the tube current in two ways. Firstly the tube current is varied based on the attenuation data acquired as part of the SPR. Secondly, attenuation in the patient is measured in real-time during the helical acquisition, where the mA is modulated to equalise the photon flux reaching the detectors during the scan. The aim of both these techniques is to keep noise levels consistent throughout the scan to allow for anatomical variations in attenuation, hence optimising image quality and patient dose.

The GE systems have a low specification CT component with many of the exposure parameters being fixed. On first glance it could be assumed that with a tube current of 2.5 mA, the dose from CTAC acquisitions would be significantly lower than the Siemens which has a mA of 20. However, taking the rotation time into account the effective mAs of each slice is much higher. Calculations using the mA and rotation time and angle of rotation illustrate that an effective mAs of 44.6 is used for each slice in these acquisitions. Performing a T-test between the two GE systems together illustrates a

statistically significant difference in dose (p=0.0002), with the four slice system giving the higher dose. Reasons for this could be due to the method of acquisition as the four-slice system acquires data helically rather than axially.

The protocol used by the Phillips Precedence gave the highest *E* of the four systems. The Phillips Precedence is a 16 slice "full diagnostic" system but as can be seen in Table 2, parameters used are significantly lower than those that would be used in diagnostic CT imaging. The opportunity for further dose reduction should be recognised by the Operator and options for dose optimisation on an individual patient basis utilised. The authors recognise that the imaging parameters used are set by the manufacturer and a departmental process of optimisation may have the potential to further reduce *E*. Manipulation of parameters such as mA, rotation time, pitch and/or acquisition method (helical or axial) have the potential to reduce dose while ensuring adequate data quality.

The phantom used in this study is representative of an adult male phantom and so risk and calculations of *E* are specific to this gender. Dose to breast and risk calculations were carried out and are shown in Table 7 however It is recognised that the risk to the female breast is likely to be different to the quoted figures due to the absence of additional breast tissue that would be present in the female phantom but as a comparison within the context of this study, some interesting results were found. This comparison highlights that although the overall lifetime biological risks associated with the CTAC exposure are much lower, organ specific risks may be comparable or higher. For example the addition of a CTAC using the Philips Precedence protocol to a 99mTc Tetrofosmin stress and rest study in a 40-49 year old increases the risk to the breast from 31 per million to 100 per million.

Conclusion

The authors recognise that local optimisation of administered radioactivity and CT imaging

parameters should be performed and actual values for *E* and risk will vary accordingly. However, as a comparison exercise this paper provides the information on the associated risks of performing CTAC. On comparison to doses and risks from the administration of radiopharmaceutical, the CTAC poses a small increase to risk especially to the older population. However, it has been shown that consideration should be given to risks to individual organs and in this case Practitioners should be aware of the increased risk to breast tissue especially in the younger patient. As per legislation justification is required and CTAC should only be used in situations that demonstrate sufficient net benefit to the patient.

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